TO STUDY THE EFFECT OF RANITIDINE ON RYLE'S TUBE ASPIRATION IN REFERENCE TO VOLUME, ph. AND CONCENTRATION IN LAPAROTOMY PATIENTS

# THESIS FOR MASTER OF SURGERY (GENERAL SURGERY)



BUNDELKHAND UNIVERSITY JHANSI (U. P.)

#### CERTIFICATE

This is to certify that the work of

Dr. KUNDAL KUMAR TAMTA, on "EFFECT OF RANITIDINE

ON RYLE'S TUBE ASPIRATION IN SPECIAL REFERENCE TO

VOLUME, pH, AND CONCENTRATION IN LAPAROTOMY PATIENTS",

which is being presented by him for M.S. (General

Surgery) Examination 1992, has been carried out in the

Department of Surgery.

He has put in the necessary stay in the department as per University regulations.

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#### CERTIFICATE

This is to certify that the work embodied in this thesis entitled, "EFFECT OF RANITIDINE ON RYLE'S TUBE ASPIRATION IN SPECIAL REFERENCE TO VOLUME, pH AND CONCENTRATION IN LAPAROTOMY PATIENTS", has been carried out by Dr. KUNDAL KUMAR TAMTA, under our guidance and supervision.

The method of work and result obtained have been checked by us from time to time and are genuine to the best of our knowledge.

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(K.K. Tamta)

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#### INTRODUCTION

Ryle's tube aspiration of gastric contents continue to draw attention in the surgical literature, for various abdominal painful conditions. In recent years the emphasis is laid on decreasing the volume of gastric contents specially in post-operative laparotomy patients.

Stress ulcer, electrolyte imbalance and acid aspiration syndrome are the serious problems in surgical practice. These all complications can be prevented by giving injection Ranitidine (a new H2-receptor antagonist). It is being widely used mostly to reduce acid contents of gastric secretion in various conditions. It may also reduce gastric fluid to some extent.

In normal individual all the secretions of gastro-intestinal tract are reabsorbed in colon barring approximately 150 cc. excreted in faeces.

In post-operative paralytic ilius due to intestinal obstruction or intestinal perforation. This fluid is not reabsorbed but collected in intestinal lumen.

After exploratory laparatomy, in these cases Ryle's

- 4. To evaluate the result of treatment.
- 5. To discuss the finding of present study in the light of available relevant literature on the subject.
- 6. To form a base-line for the further development of the technique in the contrary.

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REVIEW OF LITERATURE

#### REVIEW OF LITERATURE

GASTRIC SECRETION: Gastric juice secreted by various types of cells present in different parts of stomach.

- 1. Gastric epithelial cells: Lining the stomach are of columner type. They are filled with mucigenous granules and are responsible for lubrication of contents. About a 3rd of them generate daily by mitosis. They do not respond to acid secretagogeus.
- 2. <u>Parietal cells</u>:- These occur only in body of stomach and lie in the gastric crypts. Electron-microscopic studies show many inter-cellular canaliculi which communicate with crypt lumen. They are responsible for the secretion of isotonic Hcl. to a pH of 0.9. In a normal adult male the parietal cell population is of the order of one billion, whilst in about 2/3rd of duodenal ulcer case this way nearly doubled. In the Zollinger-Ellison Syndrome a four-fold increase has been reported. In gastric ulcer count is low.
- 3. Chief cells: These lie mainly in proximal part of gastric crypts in the fundic mucosa and are responsible for the secretion of pepsinogen.

4. Endocrine cells: - The mid zone of the gastric mucosa contains G-cells, which synthesise gastrin.

G-cells are found mainly in the gastric antrum, and their distribution differ from that of parietal cells on which gastrin acts. The number of G-cells may be increased in duodenal (but not gastric) ulcer patients, it is greatly increased in the condition known as G-cell hyperplasia. Other types of cells which secrete regulatory peptides occur in gastric mucosa. These include D-cells, which contain somatostatin, it is probable that this peptide is involved in negative feed back of gastric acid secretion.

## Basic mechanism of Hydrochloric acid secretion -

The parietal cells secrete and electrolytic solution containing 160 millimoles of hydrochloric acid per litre, which is almost exactly isotonic with body fluid the pH of this acid solution is about 0.9, thus illustrating its extreme acidity. At this pH the hydrogen ion concentration is about 3 million times that of arterial blood.

The different suggestions for precise mechanism of hydrochloric acid formation have been offered.

Chloride ion is actively transported from the cytoplasm
of oxyntic cells into the lumen of the canaliculus.
This create a negative potential of -40 to -70

millivolts in the canaliculus, which increases passive diffusion of positively changed potassium ion from the cell cytoplasm also into canaliculus thus in effect potassium chloride enter in canaliculus.

- 2. Water is dissociated into hydrogen ion and into hydroxyl ion in the cell cytoplasm. The hydroxyl ion is then actively secreted into canaliculus, in exchange of potassium ion, this active exchange process being catalysed by H<sup>+</sup>, K<sup>+</sup>, ATPase. Most of potassium ion that has been secreted along with chloride ions are reabsorbed and hydrogen takes place in canaliculus.
- 3. Water passes through the cells and into the canaliculus by osmosis, thus the final secretion from canaliculus is a solution containing hypochloric acid in concentration of 160 millimoles per litre and potassium chloride in a concentration of 17 millimoles per litre.
- 4. Finally, carbon-di-oxide, either from during metabolism in the cells or entering the cells from blood, combinds with water under influence of carbon anhydrous to form carbonic acid. This is in turn dissociated into bicarbonate ion and hydrogen ion. The hydrogen ion combine with hydroxyl ion, release in step one to form water, bicarbonate ion in turn diffuses out of the cells into blood.

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Gastric acid secretion is regulated by both nervous and hormonal mechanism. Nervous regulation being effected through parasynthetic fibres of vagus nerve as well as local intrinsic nerve plexus reflexes and hormonal regulation taking place by means of hormone gastrin.

#### Secretion of gastric Juice -

The gastric juice consists mainly of pepsin, intrinsic factors, ions and other organic solutes in dilute hydrochloric acid.

- " Conventionally three phases of secretion of gastric juices are recognised.
- 1. <u>Cephalic</u>: This is mediated by vagal activity, both from psychic arousal as demonstrated by Paulov, and reflexly from antral stimulation (Uvnas).
- 2. Gastric: Gastrin are polypeptides differing in secretogenic potency and molecular size but identical in action (Gregory) which are released from antral G-cells in response to mechanical distension of antrum, and to meat proteins. After release from the G-cells gastrin reaches the parietal cells via the systemic circulation. Secretion of acid is controlled by negative feed back; when intra-gastric pH falls below 3, due to acid secretion, the release of gastrin is inhibited. Because of the buffering capacity of mixed meal acid output is high for

half an hour after eating but falls thereafter. The role of histamine, long known as a potent stimulus of gastric acid secretion, has been a matter of controversy, but it now seems likely that gastrin acts on parietal cells through the release of histamine in conjunction with cholecystokinin, acetyl choline and possibly noradrenaline.

3. Intestinal: - Prolongation of acid secretion for some hours after feeding was originally ascribed to 'intestinal factors; but, since a mixed meal is not emptied from the stomach for several hours, it is probably due, for the most part, to prolonged gastrin release from mechanical stimulation of the antrum. The effect of chyme in intestine on gastric secretion is largely inhibitory, in order to preserve the neutral pH of duodenum. Duodenal acidification provokes secretin and bulbogastrone release, which inhibit gastric acid secretion (Grossman) and other intestinal polypeptides are probably implicated in this regulation; such poly peptides are termed 'gastrones'.

The normal average secretion of gastric juice and its contents in adults are

1. Total volume : 1200 ml to 1500 ml/day

The state of the s

- a) Water 99.45%
- b) Solid 0.55%

2. Inorganic : 0.15% i.e. Nacl, Kcl, Cacl<sub>2</sub>, calcium phosphate and bicarbonate.

Organic : 0.04%

- a) Mucin
- b) Intrinsic Factor
- c) Enzymes
  - i) Pepsin
  - ii) Gastric Renin and
  - iii) Gastric lipase
- 3. pH : 0.9 1.5 (highly acidic)

# REGULATION OF PANCREATIC SECRETION

Pancreatic secretion, like gastric secretion, regulated by both nervous and hormonal mechanisms.

However, in this case, hormonal secretion is more important.

#### NERVOUS REGULATION

When the cephalic and gastric phases of stomach secretion occur, parasympathetic impulses simultaneously transmitted along the vagus nerve to pancrease resulting in acetylcholine release followed by secretion of moderate amount of enzymes into pancreatic acini.

However, little secretion flows through pancreatic duct to intestine because only small amount of water and electrolytes are secreted along with enzymes are temporarily stored in acini.

#### HORMONAL REGULATION

After chyme enter in the small intestine pancreatic secretion become copious mainly in response to hormone secretin in addition to second hormone cholecystokinin causes greatly increased secretion of enzymes.

Normal average secretion of pancreatic juice in adult are -

- 1. Volume : 1500 ml in 24 hours
- 2. Contents
  - a) Inorganic Sodium,
    Potassium,
    Bicarbonate.
  - b) Organic -

Trypsinogen, chymotrypsinogen, procarboxypeptidase, Nucleotidases elastase, pancreatic lipase,
amylase, lacithenase.

3. pH : 0.8 - 0.83 (Alkaline).

# REGULATION OF SMALL INTESTINE SECRETION -

This is by two mechanism -

- 1) Local stimuli,
- 2) Hormonal regulation.

Local Stimuli By far most important meaning for regulating small intestine secretion are various local reflexes, specially reflexes initiate by tactile or irritative stimuli, therefore for the most part, secretion in small intestine occur simply in response, to presence of chyme in the intestine - greater the amount of chyme, greater the amount of secretion.

Hormonal Regulation - Some of the same hormones that promote secretion elsewhere in the gastro-intestinal tract also increase small intestine secretion specially secretin and cholecystokinin. Also some experiments suggest that other hormone substances extracted from small intestinal mucosa by chyme might help to control secretion. However, in general, the reflex mechanism plays an important role.

#### SECRETION OF LARGE INTESTINE -

Secretion of water and electrolyte in response to irritation, whenever a segment of large intestine becomes intensely irritated as occurs in enteritis, the mucosa then secretes large quantities of water and electrolyte in addition to normal viscid solution of mucus. This act to dilute the irritating factor and to cause rapid movement towards the anus. The usual result is diarrhoea with loss of large quantities of water and electrolyte.

Normal average secretion of succus entericus (intestinal juice) in adult are -

i) Total volume : 1000 - 2000 ml in 24 hrs.

ii) pH varies from: 6.3 - 9 (Average 8.3)

iii) Water : 98.5%

iv) Solid : 1.5%

Inorganic : 0.8% salt of sodium, potassium,

calcium and magnesium.

Organic : 0.7%

a) Activators - enteropeptidase

b) Erepsin

c) Arginase

d) Carbohydrate splitting

- Amylase

- Sucrase

- Maltase

- Lactase

Fat splitting Lipase,
Other mucin.

# SECRETION OF BILE BY LIVER -

Bile is secreted continuously by the liver rather than intermittently as in case of most other gastro-intestinal secretions but bile is stored in gall bladder until it is needed in the gut. The gall bladder is then emptied the bile into the intestine in response

to cholecystokinin. The same hormone that causes enzyme secretion by pancrease.

The rate of bile secretion can be altered in response to four different effects.

- Vagal stimulation can sometime more than double the secretion.
- 2. Secretion can increase bile secretion as much as 80% mainly by stimulating small bile duct to secrete sodium bicarbonate solution.
- 3. Greater the liver blood flow, greater the secretion.
- 4. Presence of large amount of bile salts in blood increase rate of liver secretions.

Average normal secretion of bile juice in adults are:

- i) Total volume : 500 1000 ml/day
- ii) pH : 7.7 slight alkaline
- iii) Solid : 2 11%
  - a) Inorganic salts Chloride, bicarbonate,

    phosphate, sodium, potassium,

    calcium and sodium bicarbonate.
- b) Bile salts Sodium taurocholate, Sodium glycocholate.
  - c) Bile pigment Bilirubin, Biliverdin.
    - d) Cholesterol and Lecithene.

In case of normal individual, all these secretions are reabsorbed in colon barring 150 cc. which is secreted in the faeces. In post-operative paralytic ilius due to intestinal obstruction, this fluid is not reabsorbed but collects in intestinal lumen. After operation in these cases, a Ryle's tube is put routinely to aspirate this fluid, Ryle's tube aspirate not only contain gastric juice but also Bile, pancreatic and intestinal secretions due to incompetence of pyeloric sphincter because of distension of abdomen. It is seen that very after more than 2 litres per day is aspirated which is rich in water and electrolytes.

H<sub>2</sub> receptor antagonist Ranitidine has been shown to reduce this volume of gastric juice as well as its acid pepsin contents.

This study will be direct observation of actual effect of Ranitidine on gastric juice volume and contents.

Ranitidine, a histamine H<sub>2</sub>-receptor antagonist, is now well established as a potent inhibitor of gastric acid secretion effective in the treatment and prophylaxis of gastro-intestinal lesions aggrevated by gastric acid secretion.

Therapeutic trials involving several thousands of patients with peptic ulcer disease confirm that Ranitidine 300 mg daily administered orally in single

or divided doses is at least as effective as Cimetidine 800 to 1000 mg daily in increasing the rate of healing of duodenal and gastric ulcers. Similar doses of Ranitidine has been shown to relieve the symptoms of reflux oesophagitis and heal or prevent gastro-intestinal damage caused by ulcerogenic drugs. Ranitidine 150 mg orally at night maintains ulcer healing in long term. Ranitidine has also demonstrated good results in treatment of Zollinger Ellison Syndrome and in prevention of aspiration pneumonitis when given prior to surgery and to pregnant women at full term.

It may also have a place in the management of acute upper gastro-intestinal bleeding and in the prevention of stress ulcer in the intensive care setting although this area requires further investigations. The drug is very well tolerated and is only infrequently associated with serious adverse reactions or clinically significant drug interactions. Even at high doses ranitidine appears to be devoid of antiandrogenic effect.

Ranitidine is clearly comparable or superior to the most other anti-ulcer agents in the treatment and prevention of a variety of gastro-intestinal disorders associated with gastric acid secretion. With its favourable efficacy and tolerability profiles, ranitidine must be considered a first line agent when suppression of gastric acid secretion is indicated.

## VARIOUS WORK HAS BEEN DONE ON RANITIDINE

Effect on gastric acid secretion non-comparative and placebo controlled studies -

Studies in healthy volunteers reviewed previously by Brogden et al (1982) demonstrated that ranitidine, by oral or intravenous routes, produces a dose-dependent inhibition of gastric acid secretion stimulated by pentagastrin, peptone, a steak meal or histamine.

The newer technique of ambulatory intragastric pH-metry has since been widely used to monitor the physiological pattern of gastric acid secretion and effects of ranitidine on acid output. There is a circadian pattern to gastric acid secretion with periods of low pH in early evening the first half of night, late morning and afternoon.

In the second half of night or early morning, gastric pH normally rises and periods of high pH follow each meal, presumably the result of nutralisation by food (Coppens et al, 1988). Comparing the pattern of gastric pH in normal subjects (n = 40) and patients with endoscopically proven active ulceration (n = 46) Merki et al (1986) noted that patients with ulcer disease have a lower median 24-hour pH (1.3 vs 1.6 in healthy subjects; P \( \subsection 0.0005 \)) and show a less pronounced rise in pH in the early morning and after meals. Similarly

Kapur and Bardhan (1988) found that normal subjects (n = 22) and patients with healed duodenal ulcer (n = 55) had essentially identical 24 hour pH profiles but that patients with active duodenal ulcer (n = 30) spent 80% of time between 2400 and 0850 hours at pH \( \subseteq 2 \) compared with 46% and 59% for healthy and healed subjects. respectively. There was no difference in acid output between the 3 groups during the day (0850 to 2499 hours).

Using pH-metry, Fimmel et al (1985) produced a 24 hour pH profile showing the effect of 2 oral doses of ranitidine 150 mg or 300 mg at 1200 and 2200 hours in 25 healthy subjects. Compared with placebo, ranitidine 150 mg twice daily raised the percentage of pH readings greater than 4 by 38% and ranitidine 300 mg twice daily by 48%. The 24 hour mean pH and area under the gastric pH time curve were also increased significantly (P \( \times 0.05 \)) compared with placebo. Ranitidine 300 mg orally as a single dose at 1800 or 2200 hours also decreased the percentage of highly acidic pH readings and decreased the mean 24 hour hydrogen ion (H+) activity and area under the H+ activity time curve in 6 normal volunteers as compared with placebo (Coppens et al. 1988).

In this latter study, a significant (P \( \sigma 0.05 \)
to 0.01) difference was noted between the degree of H<sup>+</sup>
activity inhibition achieved by early (1800 h.) versus
late (2200 h.) administration of ranitidine. Similarly

in 12 healthy volunteers given either placebo or ranitidine 300 mg orally at 1800 or 2200 hours in double-blind double-dummy design, early administration of ranitidine resulted in a significantly (P \( \times 0.012 \)) greater reduction in the duration of highly acidic readings (pH \( \times 1.5 \)) recorded over a 24 hour period (Merki et al, 1987).

In 12 patients with healed duodenal ulcer, 24 hour's treatment with ranitidine 150 mg at 0900 and 2100 hours or 300 mg at 2100 hours decreased the mean 24 hour. H+ activity by 63% and 62% respectively (P / 0.05 compared with placebo). The effect of once or twice daily ranitidine was greatest on nocturnal acid output (decreased 84% and 73% respectively; P / 0.05). Although the twice daily schedule caused a 29% decrease in H+ activity from 1300 h. onwards, no significant day time effect was noted for a single bed time dose (Gledhill et al. 1983). In 8 patients with duodenal ulcer in remission 7 days' maintenance therapy with ranitidine 150 mg at bed time produced a 42% decrease in mean 24 hour intragastric acidity compared with baseline which was due to a significant (P \( 0.001 \) decrease in nocturnal acidity. As in the previous study, day time pH was not affected by the single bed time dose of ranitidine (Santana et al. 1984).

Comparison of early (1800 h) with late (2200 h) administration of ranitidine 300 mg in 8 patients with

healed duodenal ulcer showed that early administration produced greater inhibition of 24 hour H+ activity (P  $\angle$  0.05) and over the nocturnal period (P  $\angle$  0.01). As in the previous studies the single bed time dose of ranitidine had no effect on day time H+ activity. While the effect of ranitidine administered at 1800 h. was significant (P  $\angle$  0.05) the 'day time' period was defined as 0800 to 2200 hours and is not comparable drug free interval (Coppens et al. 1988).

The reason for poor diurnal pH control with ranitidine is unclear although the secretory response to meals consumed during waking hours may be involved. The stimulus of food appears able to surmount ranitidine inhibition of gastric acid secretion (Frislid & Berstad, 1984; Kempf et al, 1988) even though food in stomach does not alter plasma ranitidine concentrations nor does it increase the concentration of ranitidine detectable in gastric juice (Frishlid & Berstad, 1985). Food does however stimulate various physiological mechanisms controlling the intra-gastric environment, perhaps leading to changes in the gastric mucosa, which by pass the overwhelm the H<sub>2</sub> receptor. Clarification of these mechanisms may benefit patient's who demonstrate "ranitidine resistance".

#### COMPARISONS WITH CIMETIDINE -

In a double blind study in 30 normal volunteers, single oral doses of ranitidine 300 mg or cimetidine 800 mg administered at 1900 hours. Significantly (P / 0.0005) decreased 24 hour acidity compared with placebo but the acid inhibitory effect of ranitidine was significantly (P / 0.001) greater than the effect of cimetidine (decreased 87% and 60% respectively) (Merki et al, 1988 b). Similarly, in a study of 25 healthy subjects, 2 doses of ranitidine 150 mg at 1200 and 2200 hours were more effective than 2 doses of cemitidine 400 mg at increasing the percentage of intragastric pH readings greater than 4 (38% and 24% respectively). Ranitidine 150 mg twice daily and cimetidine 400 mg 4 times daily were equally effective at increasing the percentage of high pH readings ( 7 3, 4 and 5) and at increasing the area under the gastric pH time curve (Fimmel et al, 1985).

The same results were obtained after 2 doses of ranitidine 300 mg or cimetidine 1600 mg administered at 1800 h daily to 8 patients with duodenal ulcer in symptomatic remission (Deakin et al, 1987). The effects of ranitidine 300 mg and cimetidine 1600 mg were not significantly different as regards nocturnal and day time acidity and both treatments produced a significantly (P \( \subseteq 0.05 \)) greater inhibition of hydrogen ion activity

than did cimetidine 800 mg. Ranitidine 150 mg twice daily was compared with cimetidine 200 mg 3 times daily and 400 mg at bed time in 10 patients with duodenal ulcer in remission. Compared with placebo treatment, ranitidine increased the percentage of nocturnal aspirate samples greater than pH 5 by 54% (P  $\angle$  0.001) and cimetidine by 39% (P  $\angle$  0.001). Ranitidine had a statistically greater effect on mean nocturnal acid output (P  $\angle$  0.05) and on mean 24 hour intra-gastric hydrogen ion activity (P  $\angle$  0.001) than did cimetidine at these dosages (Walt et al. 1981 a).

In 6 patients with duodenal ulcer treated in cross over fashion, intravenously administered ranitidine 50 mg every 6 or 8 hours or cimetidine 300 mg every 6 hours were not significantly different at raising the mean fasting gastric pH over the 10 hour study period. The 6 or 8 hourly regimens of ranitidine produced equivalent pH profiles and maintained the intra-gastric pH above 5 more consistently than did the cimetidine treatment (Peterson & Richardson, 1986).

As prophylaxis against the stress induced gistro-intestinal bleeding, intravenous ranitidine appeared to be more effective than cimetidine in maintaining intra-gastric pH within a "safe" range (pH 3.5 to 5) (More et al. 1985; Reid and Bayliff, 1986). In the double-blind study by Reid and Bayliff (1986).

a continuous infusion of either drug was employed for upto 7 days to maintain the intra-gastric pH above 5. A statistically (P / 0.05) greater incidence of poor control ( 7 25% of pH measurements / 5) occured in patients receiving cimetidine 50 mg/h (1200 mg/day) compared with ranitidine 12.5 mg/h (300 mg/day). In the study by More et al (1985), successful treatment defined as continuous intra-gastric pH 74, was achieved in 10 of 20 patients administered ranitidine upto 100 mg every 4 hours compared with 5 of 28 patients administered cimetidine upto 400 mg every 4 hours.

#### COMPARISONS WITH FAMOTIDINE

Ranitidine 300 mg orally and Famotidine 40 mg orally were administered as single evening doses to 30 healthy volunteers monitored with intra-gastric pH probes in a double blind placebo controlled cross over study. The median 24 hour acidity of placebo, ranitidine-and famotidine-treated patients was 25 m mol/L, 3.2 m mol/L and 2.5 m ml./L, respectively. The inhibition produced by ranitidine and famotidine was not significantly different (Merki et al, 1988 b).

patients with healed duodenal ulcer under similar study conditions, although the onset and duration of inhibition produced by famotidine 40 mg were earlier and longer, respectively compared with ranitidine 300 mg. Neither

drug significantly affected day time pH but, through the night, famotidine maintained high pH values (pH 6 to 8) for longer periods, conferring a pharmaco-dynamic if not a therapeutic advantage for this agent (Savarino et al, 1987).

In a double blind study of 20 critically ill adults ranitidine 50 mg and famotidine 10 mg every 6 or 8 hours were compared as intra-venous prophylactic treatment of stress induced gastro-intestinal bleeding.

During 7 days of treatment, ranitidine and famotidine were equally effective in maintaining intra-gastric pH above 4 (60 and 63% of pH measurements 74, respectively) and duration of low pH periods did not differ between treatment groups (Dammann et al. 1985).

#### COMPARISONS WITH OTHER TREATMENTS -

In small double-blind placebo-controlled studies in normal volunteers, ranitidine was compared with the histamine H<sub>2</sub>-antagonists roxatidine acetate and nizatidine. Ranitidine 300 mg orally at bed time was as effective as roxatidine acetate 150 mg at bed time, raising the median nocturnal pH from 1.4 to 6.7 and 6.65, respectively (Merki et al, 1988 a). Compared with ranitidine 300 mg orally at bed time, nizatidine 150 mg or 300 mg orally at bed time reduced median 24 hour acidity to a similar degree (-54, -45, and -49%, respectively) (Lanzon-Miller et al, 1987 a). Missale et al (1987) confirmed equal

suppression of fasting gastric acid output by ranitidine 150 mg and nizatidine 150 mg but noted a greater and more prolonged suppression of pentagastrin-stimulated acid secretion in ranitidine treated patients.

In a retrospective comparison of gastric acid inhibition observed in separate studies of ranitidine 300 mg or cimetidine 1000 mg per day for 24 hours and Omeprazole 30 mg daily for 7 days in small groups of patients with a history of duodenal ulcer, Omeprazole was more potent with regard to decreasing the mean 24 hour hydrogen ion activity, increasing the median 24 hour pH and increasing the percentage of aspirate samples greater than pH 3 (Walt et al, 1983). In a cross over study involving 28 days' treatment with ranitidine 150 mg twice daily or Omeprazole 20 mg daily in 12 patients with active duodenal ulcer, omeprazole induced and maintained profound acid suppression throughout both day and night. Ranitidine produced a statistically significant (P \_ 0.001) decrease in intra-gastric acidity between 2200 and 1900 hours but the decrease was less than that obtained with omeprazole (Lanzon Miller et al, 1987 b).

In a single dose placebo-controlled study of
6 patients with symptomatic duodenal ulceration,
ranitidine 150 mg orally was a more potent inhibitor of
meal stimulated gastric secretion than was the antimuscarinic agent pirenzepine 50 mg orally (gastric output)

decreased 69 and 39% respectively) (Lazzaroni et al, 1986). In this study, concurrent administration of ranitidine 150 mg and pirenzepine 50 mg achieved near total inhibition of acid secretion, an interaction previously noted for cimetidine and pirenzepine and for ranitidine and pirenzepine in intravenous form (for a review see Poch and Londong, 1985).

Intra-gastric pH changes produced by ranitidine (300 mg orally at bed time) and by highly selective vagotomy (4 to 13 weeks after surgery) were compared with placebo treatment in 16 patients with duodenal ulcer using ambulatory intra-gastric pH monitoring. The median 24 hour H+ concentration were reduced by 68% in vagotomy patients and 50% in ranitidine treated patients. While the net result were not statistically different, the 2 forms of treatment had different effects on day and night acid output. Ranitidine produced a more profound inhibition of nocturnal acidity (-89% vs -57% for vagotomy; P \( 0.01 \) whereas the effect of highly selective vagotomy was more profound during the day (-80% vs -30% for ranitidine; P / 0.0001) (Rogers et al, 1988).

# EFFECT ON SERUM GASTRIN CONCENTRATION -

Earlier studies reviewed by Brogden et al (1982) did not demonstrate a significant effect of ranitidine on serum gastrin levels; however, a number of more recent investigations report statistically significant elevation of serum gastrin concentrations. In a study which measured intra-gastric pH and plasma gastrin concentrations simultaneously over 24 hours, oral ranitidine 150 mg twice daily increased the median integrated 24 hour gastrin concentration significantly (P \( \subseteq 0.001 \)) in 12 patients with healed duodenal ulcer, from 328 p mol/L.h before to 799 p mol/L.h after 28 days' treatment (Lanzon Miller et al, 1987 b).

In 23 patients with duodenal ulcer disease treated with ranitidine 150 mg orally twice daily for 8 weeks (Mohammed et al, 1983) and in a further 22 duodenal ulcer patients similarly treated for 1 year (Lombardo et al, 1983), fasting serum gastrin level tended to rise during treatment but returned to base line after ranitidine was discontinued. In a preliminary report, Delle Fave et al (1987) observed that 23 of 170 duodenal ulcer patients developed basal serum gastrin concentrations in excess of 150 ng/L during 8 to 12 weeks of unspecified H<sub>2</sub>-antagonist treatment, but that only 9% of patients still had an elevated serum gastrin level 1 week after stopping treatment and this number declined to 3% after 1 month.

The integrated gastrin response to meals was investigated in 6 patients with asymptomatic gastro-esophageal reflux disease given ranitidine 150 mg twice

daily, cimetidine 300 mg 4 times daily or placebo for 1 week in cross over fashion (Mahachai et al, 1985). Basal serum gastrin concentrations were similar for all treatments but the increase in gastrin concentration following breakfast, lunch and dinner was some what greater and more prolonged following treatment with ranitidine or cimetidine. Statistical significance between placebo and active treatment groups was demonstrated only for the 7 hour integrated gastrin response to the evening meal. Ranitidine 150 mg twice daily for 6 weeks in 25 patients with active reflux oesophagitis did cause a significant rise in the integrated gastrin response to a standard breakfast (from 4268 to 7198 ng/L. 90 minutes; P \( 0.05 \). In 5 of these patients oesophageal healing during placebo treatment was not associated with a change integrated gastrin response but cross over to 6 weeks treatment with ranitidine significantly (P / 0.05) increased the integrated gastrin response (Sherbaniuk et al, 1983).

The mechanism of ranitidine induced increases in serum gastrin concentration is unclear. Some studies have found an inverse relationship between mean 24 hour intra-gastric hydrogen ion activity and serum gastrin concentration which suggests that gastric anacidity is stimulus for gastrin secretion (Lanzon-Miller et al., 1987 b, c). Other investigators (Mahachai et al., 1985)

have failed to confirm this relationship, however and the mechanism remains unresolved.

## EFFECT ON PEPSIN ACTIVITY

A dose dependent decrease in pepsin output due mainly to a decrease in the volume of gastric secretion rather than a decrease in pepsin concentration has been reported in healthy subjects given single doses of ranitidine intravenously (Domschke et al, 1980; Lebert et al, 1981 b) or orally (Mahon et al, 1980; Muller-Lissner et al, 1981) and in patients with duodenal ulcer (Konturek et al, 1980; Peden et al, 1979). Stimulated pepsin secretion has generally been less markedly decreased by ranitidine than has acid secretion in healthy subjects (Domschke et al, 1980; Frislid and Berstad, 1986; Lebert et al, 1981 b) and in patients with duodenal ulcer (Konturek et al, 1980; Peden et al, 1979).

As gastric pH rises above 4 the conversion of inactive pepsinogen to proteolytic pepsin is reduced and at pH level of neutrality or alkalinity, the enzymes are irreversibly denatured. Hence pepsin activity declines secondary to ranitidine induced anacidity even as ranitidine suppresses pepsin output.

### EFFECT ON GASTRIC MUCUS -

The effect of ranitidine 300 mg daily for 4 weeks on gastric mucus has been compared with that of

cimetidine or famotidine treatment in 12 and 20 duodenal ulcer patients respectively (Guslandi et al, 1981, 1987 b) whereas both cimetidine and famotidine reduced the ratio of neutral to total mucoproteins - an index developed by these investigators which correlates the constituents of gastric mucus to the viscoprotective properties of gastric mucus coating ranitidine had no effect. Sarosiek et al (1984) described an increased output of glyceroglucolipid (which potentially contributes to the inhibition of Ht back diffusion and to pepsin regulation in the gastric and duodenal ulcer patients) secondary to treatment with ranitidine 150 mg twice daily for 4 weeks. Gabryelewicz et al (1987), in a placebo-controlled trial of 60 non-steroidal anti-inflammatory drug users, noted a decrease in the soluble sialic acid content of gastric juice secondary to ranitidine 150 mg twice daily which, the authors suggest, may reflect a beneficial thickening of the gastric mucosal barrier. Conversion of soluble gastric mucus to a tenacious gel was observed following an intravenous infusion of ranitidine (0.7 mg/kg/h) to 10 patients with duodenal ulcer (Gabryelewicz et al, 1983). During the infusion, significant decreases in pentagastrin stimulated gastric volume acid secretion and pepsin secretion were obtained but mucus output did not decrease.

## EFFECT ON GASTRO-INTESTINAL MOTILITY -

intestinal motility complicated by the variety of methodologies employed and by the use of non-comparable study populations (normal subjects vs patients with active ulcer disease vs patients with healed lesions).

Motor activity within the gastro-intestinal tract is phasic and may be influenced by various inhibitory or stimulatory factors including meal osmolarity, pH, fat, or caloric content by motilin, gastrin, histamine, secretin, cholecystokinin octa peptide, gastric inhibitory polypeptide, acetylcholine, or pancreatic polypeptide (Lam et al, 1982; Myren et al, 1986). Our understanding of 'normal' gastro-intestinal motor activity is incomplete but the process is clearly complex with the potential for interference at many levels.

# LOWER OESOPHAGEAL SPHINCTER FUNCTION -

Bertaccini and Coruzzi (1982) noted a doserelated increase in lower oesophageal sphincter pressure
(LOSP) measured in healthy subjects after single intravenous bolus injections of ranitidine 0.5 or 1 mg/kg
(P \( \subseteq 0.01 \) compared with saline injection). Contrary to
these results, in a double blind placebo controlled trial
in 9 healthy subjects, an intravenous infusion of
ranitidine 0.16 mg/kg/h. significantly (P \( \subseteq 0.05) \)
decreased LOSP measured before a meal. In this study

the effect of ranitidine on LOSP did not differ from that of placebo post prandially, except for a significant (P \( \sigma 0.05 \)) decrease 120 to 150 minutes after the meal - the last observation period of the study (Smout et al, 1985).

In the latter study by Smout et al (1985) continuous manometry was used in an effort to distinguish between drug induced effects on LOSP and normal physiological fluctuation. Using a similar technique in a double-blind placebo controlled trial in 6 healthy subjects, Baldi et al (1984) detected no significant change in LOSP after a single oral dose of ranitidine 150 mg either before or after a meal. Other investigators, using intermittent measurements obtained by pull through manometry, found no consistent change in the LOSP of healthy subjects after a single oral dose of ranitidine 150 mg (n = 10) (Wallin et al, 1983). On 3.5 days' treatment with ranitidine 100 mg orally 3 times daily (n=10) (Denis et al, 1981). Similarly, there was no consistent LOSP response to a single intravenous injection of ranitidine 50 mg in 15 patients with gastrooesophageal reflux disease (Meyrick Thomas et al, 1983). Thus the pharmacodynamic data regarding the effect of ranitidine on lower oesophageal sphincter pressure are equivocal. Larger well designed trials utilizing continuous measurement techniques are needed, particularly in patients with impaired sphincter function, before conclusions can be made regarding this aspect of ranitidine treatment.

## GASTRIC EMPTYING -

Gastric emptying is faster in patients with active duodenal ulcer compared with normal subjects and does not correlate with the rate of basal or pentagastrin stimulated acid output (Jonderko, 1987; Lam et al, 1982). Gastric motality may normalise in patients whose duodenal ulcers are healed (Moore et al, 1985). However, a controlled prospective evaluation of the same patients during active and inactive phases of disease will be needed to confirm this.

Using fibre optic transducers, Myren et al (1986) measured muscle activity of the antrum and duodenum in 20 healthy fasting subjects given ranitidine 150 mg twice daily for 2 days in a double-blind placebocontrolled cross-over study. Compared with placebo treatment ranitidine induced a significant (P \( \subseteq 0.03 \)) increase in the duration of maximal pressure periods, an increase in cyclic length and a significant (P \( \subseteq 0.03 \)) decrease in cyclic displacement. The investigators suggest that these opposing effects balanced each other with the net result that gastric motility is not altered by ranitidine.

Using radio-isotope labelled meals fed to healthy volunteers, investigators have determined the rate of passage of solids and liquids from stomach to duodenum after treatment with a single oral dose of ranitidine 150 or 300 mg (Houghton & Read, 1987; Jonderko, 1988) or a single intravenous dose of ranitidine 50 mg (Corinaldesi et al, 1984; Scarpignato et al, 1988). In these studies, the measurement period coincided with expected peak plasma ranitidine concentrations. A significant (P \( \sum\_{0.05} \)) delay in the emptying rate of liquid meal from 24 to 48 minutes after ingestion was observed by Houghton and Read (1987) in 10 normal subjects given ranitidine 300 mg orally. No effect was found on the rate of emptying of a solid meal at any time. A significant (P / 0.05) increase in mean transit time was noted in 28 subjects given ranitidine 300 mg as a single oral dose (Jonderko, 1988). Ranitidine 150 mg also prolonged mean transit time although not a statistically significant degree and both doses tended to prolong the half-emptying time (P not significant). A 50 mg intravenous bolus dose of ranitidine increased (P ∠ 0.02) the gastric emptying rate of mixed meal in 8 volunteers (Scarpignato et al, 1988) but the same dosage delayed (P / 0.05) gastric emptying of solids and liquids in a double blind cross-over study involving 18 volunteers (Corinaldesi et al, 1984) and in a less well controlled study of 7 volunteers (Scarpignato and Bertaccini, 1982).

Two studies each involving 6 healthy volunteers given a single oral dose of ranitidine 150 mg found that ranitidine increased the rate of gastric emptying as compared with placebo treatment when measured with a Heidelberg capsule (radio-tolemetric indicator of gastro-intestinal pH) (Mojaverian et al. 1987) or with indissoluble pellets (radiographic marker) (Bertrand et al. 1984).

In the later study the same radiographic technique revealed a similar increase in rate of gastric emptying in 12 patients with active duodenal ulcer (Bertrand et al, 1984). A single dose of intravenous ranitidine 50 mg 30 minutes prior to fluroscopy significantly increased the rate at which barium labelled liquids (P \( 0.001 \)) and solids (P \( 0.005 \)) emptied from the stomachs of 32 patients with active duodenal ulcer in double blind placebo controlled cross-over trial (Huscher et al, 1984). However, in another double blind cross-over evaluation involving 15 patients with active duodenal ulcer, 2 weeks treatment with ranitidine 150 mg orally twice daily elicited no change when compared with placebo regarding the emptying of either solid or liquid components of a radio-labelled meal (Corinaldesi et al, 1984). In a larger study of 45 patients with active duodenal ulcer, both single dose oral treatment with ranitidine 150 to 300 mg and 2 weeks' continuous treatment with ranitidine 150 mg, twice daily or 300 mg at bed time

resulted in significant (P  $\angle$  0.05 to 0.005) increases in the mean transit time of a radio-labelled meal. All treatment tended to prolong the half emptying time and thus delay emptying but only the 300 mg doses produced a statistically significant (P  $\angle$  0.005) effect. Endoscopic evidence of early ulcer healing after 2 weeks of ranitidine therapy in these patients did not correlate with gastric emptying rate.

Like the data on lower oesophageal sphincter tone, data on gastro-duodenal muscle activity are equivocal. Larger studies involving patients matched prospectively for base line gastric emptying rate, gastrin response, acid output and baseline, inter-digestive migratory motor complex are needed to clarify the effects of ranitidine and define the relationship between motility modifying effects (if any) and the course of duodenal ulcer healing.

\*\*\*

### MATERIAL AND METHODS

The present study has been conducted at M.L.B.

Medical College & Hospital, Jhansi (U.P.) from April 1990

to May 1991. The study included 60 adult patients

subjected to varied emergency abdominal surgical

procedures.

The criteria of selection of the patients has been the presence of signs and symptoms of either acute intestinal obstruction or intestinal perforation.

Cases in whom the diagnosis was clinically evident and proved by radiological and laboratory investigations, were operated. For the purpose of comparative study, patients were randomly divided into four groups of 20 each as follows:

- Group A: received no test drugs in first 24 hour of laparotomy as a control group.
- Group B: received 2 injections of ranitidine 50 mg each 12 hourly intravenously.
- Group C: received no test in first and second 24 hours

  (48 hours) of laparotomy.

Group D: received 4 injections of ranitidine 50 mg
each 12 hourly upto 36 hours of laparotomy
intravenously.

All these cases were studied in following manner.

# I. Detailed History :

- Particulars of the patient it included name, age, sex, caste, address.
- Family history particular history regarding the tuberculosis.
- 3. Past history history of previous abdominal operation for intestinal obstruction and intestinal perforation.
- 4. Personal history Enquiry was made into personal habits of patients regarding the following point, Bowel habit, appetite and type of diet taken.
- 5. Social history history regarding the social and economic status, about living conditions.
- 6. Complaints with duration They were recorded in following manner:
  - (i) Pain duration, nature, site.
  - (ii) Vomiting Frequency, amount, colour.
  - (iii) Constipation Absolute and partial, duration.

- (iv) Fever regular, irregular, high, low, diurnal variation.
  - (v) Distention of abdomen.

# II. Physical Examination:

- General Examination general built, pulse, temperature, blood pressure, anaemia, jaundice, lymphnode enlargement and oedema.
- Systemic Examination examination of cardiovascular, respiratory and nervous systems.
- 3. Examination of Abdomen was recorded in following manner -
  - (a) Inspection contour of abdomen, superficial veins, scar of previous operation, tatto marks, umbilicus.
  - (b) Palpation feeling of abdomen, presence of any tenderness and rigidity and its distribution, any organomegaly.
  - (c) Percussion evidence of intra-peritoneal fluid.
  - (d) Auscultation presence or absence of bowel wounds and their nature.
  - (e) Rectal and vaginal examination.

# III. INVESTIGATION

- A. Following investigations were carried out in all cases:
  - (1) Blood Total & Differential, W.B.C. count, Haemoglobin.
  - (2) Urine Albumin, sugar, microscopic examination.
  - (3) Blood urea and Blood sugar.
  - (4) Plain X-ray abdomen.

All these patients were kept for emergency operation and Ryle's tube was routinely put. After immediate operations Ryle's tube aspiration started and kept for volume, pH and concentration -

- Volume of the Ryle's tube aspiration on first 24 hours is measured by help of measuring flask,
- Its pH was determined immediately with the help of pH indicator paper and watching against a standard colour scale,
- Concentration of solid and liquid were calculated by evaporation of liquid content in laboratory.

After immediate first 24 hours, injections of ranitidine 50 mg 2 ampulæs 12 hourly given. The volume, pH, concentration was measured as first 24 hours in Group B.

In group C cases, Ryle's tube put volume, pH and concentration, measured for 48 hours of laparotomy.

In Group D, injections of Ranitidine 50 mg given intravenously immediately after operation and continued 36 hours of the operation 12 hourly intravenously (these were 4 ampules). Volume, pH and concentration were measured after 48 hours of the operation.

\*\*\*\*

### **OBSERVATIONS**

The present study was conducted on a series of 60 patients of either sex and adult age group, admitted to M.L.B. Medical College and Hospital, Jhansi, during session 1990-1991. 41 males and 19 females constituted the whole group of patients.

 $\begin{array}{ccc} \underline{\text{TABLE}} & -1 \\ \\ \underline{\text{Distribution of patients according to sex.}} \end{array}$ 

Sex		nagogungas salabanan kinyabahanan kecamanan	No.	of	patients	
Male					41	
Pemale					19	
Total				<u> </u>	60	

Table 2 reveals distribution of patients according to their age in years. Maximum number 26 (43.39%) patients belonging to the age group 40-49 years. 22 (36.66%) patients were found in age group

30-39 years, while 8 (13.33%) patients were belonging to age group 20-29 years. Two (3.34%) patients were examined in age group 10-19 years and lowest number of patients i.e. 2 (3.34%), as just previous one, belonging to age group 50-59 years.

TABLE - 2

Distribution of patients according to age.

Age group (years)	No. of patients	Percentage
10 - 19	2	3,34
20 - 29	8	13.33
30 - 39	22	36.66
40 - 49	26	43.33
50 ~ 59	2	3.34
rotal	60	100.00

Table 3 reveals distribution of patients according to their age in years with disease. Maximum number 16 belongs to age group 40-49 years suffering from intestinal obstruction and in the same age group, patients with maximum number 10 suffering from intestinal perforation. 12 patients of acute intestinal obstruction

and 10 patients of intestinal perforation were found in age group 30-39 years, while 4 patients of acute intestinal obstruction and 4 patients of intestinal perforation were belonging to age group 20-29 years.

One patient of acute intestinal obstruction and 1 patient of intestinal perforation was belonged to the age group 10-19 years. Two patients of acute intestinal obstruction were belonged to age group 50-59 years, while no patient of intestinal perforation was found in the same age group.

<u>TABLE - 3</u>

Distribution of patients according to disease.

		· · · · · · · · · · · · · · · · · · ·	
Age group (years)	No. of patients	Acute intestinal obstruction	Intestinal perforation
10 - 19	2	1	1
20 - 29	8	4	4
30 - 39	22	12	10
40 - 49	26	16	10
50 - 59	2	2	-
Total	60	35	25

Table 4-A & 4-B: 13 patients belonging to Group C, Ryle's tube aspirate shows maximum volume range 2000 - 3000, average 2500 ml in acute intestinal obstruc. or and in the same age group 7 patients of intestinal afforation showing maximum volume range 2200-2500, average 2350 ml, 12 patients belonging to Group D, maximum volume Ryle's tube aspirate range was 1500-2000, average 1750 ml, in acute intestinal obstruction, but in 8 cases of intestinal obstruction, range was 1800-2500, average 2150 ml. 10 patients of acute intestinal obstruction of Group A, Ryle's tube aspirate volume range was 1000-2000, average 1500 ml, whereas in 10 patients of intestinal perforation of same group showed Ryle's tube aspirate volume range 1500-2000 ml, average 1750 ml.

The lowest Ryle's tube aspirate volume range 800 - 1600, average 1200 ml, was found in 10 patients of acute intestinal obstruction of Group B, and in the same group Ryle's tube aspirate volume range 1200-2000, average 1600 ml, was found in 10 patients of intestinal perforation.

TABLE - 4-A

Showing volume of Ryle's tube aspiration in different groups in 24 hours.

		Acute I	Acute Intestinal Obstruction	truction	Intest	Intestinal Perforation	r o
Group	No. of	No. of	Ryle's Tube Aspirate Volume in ml.	Aspirate	No. of	Ryle's Tube Aspirate Volume in ml.	Aspirate in ml.
	Co instance	patients	Range	Average	patients	Range	Average
4	50	10	1000-2000	1500	10	1500-2000	1750
M	Same		800-1600	1200	2	1200-2000	1600
Total	20	10		ribijanikujiretur-eleti detilijanip-enemilijinigis-eto	10		Material programme of the state

TABLE - 4-B

Showing volume of Ryle's Tube Aspiration in different Groups in 48 hours.

		Acute 1	Acute Intestinal Obstruction	struction	Inte	Intestinal Perforation	ation
Group	Number of	No. of	Ryle's Tube Aspirate Volume in ml.	Aspirate in wl.	No. of	Ryle's Tube Aspi Volume in ml.	Ryle's Tube Aspirate Volume in ml.
		patients	Range	Average	bacrencs	Range	Average
U	20	13	2000-3000	2500	7	2200-2500	2350
А	20	12	1500-2000	1750	505	1800-2500	2150
Total	40	25		And the second s	15		

Table 5-A & 5-B: In Group A, the critical limit of Ryle's tube aspiration taken as 100%. In Group B, taken as test group, showed 80%, in 10 cases of acute intestinal obstruction, while in 10 test cases of intestinal perforation 91.42%. In Group C, the critical limit of Ryle's tube aspirate taken as 100%. In Group D taken as observed group showed 70% in 12 cases of acute intestinal obstruction, while in 8 cases of intestinal perforation 91.48%.

TABLE - 5-A

Showing number of cases and their percentage of volume in 24 hours.

Group	Number of patients	obs Ryle's	intestinal truction tube aspirate me (ml.)	perfor Ryle's t	
		No.of Cases	Percentage	No.of cases	Percentage
A	20	10	100	10	100
В	Same patients	21	80	N	91.42
Total	20	10		10	

TABLE - 5-B

Showing number of cases and their percentage of volume in 48 hours.

Group	Number of patients	Obst Ryle's t	intestinal cruction cube aspirate ne (ml.)	Perf Ryle's	estinal oration tube aspirate ume (ml.)
Approximation and a substance interconstitution	Minimizati andiline (Minimizationia) ilianoisi kanada kanada kanada kanada kanada kanada kanada kanada kanada k	No.of cases	Percentage	No.of	Percentage
C	20	13	100	7	100
D	20	12	70	8	91.48
Total	40	25		15	

Table 6-A & 6-B: Patients belonging to Group-A, were those who presented as an acute intestinal obstruction and intestinal perforation were 10 and 10 in number respectively. pH range 2-3, average 2.5. Group B comprises of same patients, out of 20, 10 belonged to acute intestinal obstruction and 10 patients to intestinal perforation. pH range 5-6, average 5.5. Group C comprises of 20 patients, 13 cases of acute intestinal obstruction and 7 cases of intestinal perforation. pH range 2-3, average 2.5. But Group D comprises of 20 patients, 12 acute intestinal obstruction and 8 intestinal perforation. pH range 6-7, average 6.5.

TABLE - 6-A

Showing pH of Ryle's Tube Aspiration in different groups in 24 hours.

Group	Number of	Acute Obs	Intest tructi			estina: oration	
	patients	No. of patients	Ryle Aspi Range	s Tube rate pH Average	No. of patients	Ryle Aspin Range	s Tube rate pH Average
Α	20	10	2 - 3	2.5	10	2 - 3	2.5
В	Same patients	**	5 - 6	5.5	84	5 - 6	5.5
Total	20	10		ar-mia challantesia-variarita estatuan estatuan estatuan	10		

TABLE - 6-B

Showing pH of Ryle's Tube Aspiration in different Groups in 48 hours.

Group	Number of patients		Acnir			Aeni	
		pacrenc		Average		Range	Average
С	20	13	2 - 3	2.5	7	2 - 3	2,5
D	20	12	6 - 7	6.5	8	6 - 7	6.5
Total	40	25			15		

Table 7-A & 7-B: In Group A, the critical limit of Ryle's tube aspirate pH taken as 100%. In group B taken as a test group, has been seen in 10 cases of acute intestinal obstruction 220%, while in 10 cases of intestinal perforation 220%. In group C, the critical limit of Ryle's tube aspirate pH taken as 100%. In group D taken as an observed group has been seen in 12 cases of acute intestinal obstruction 260%, while in 8 cases of intestinal perforation 260%.

TABLE - 7-A

Showing number of cases and their percentages of pH in 24 hours.

Group	Number of		ntestinal ruction		stinal oration
or orb	patients	Ryle's	tube te pH	Ryle	s tube ate pH
adigitalistika ilminik sentendikendike	- consiste die Soulie telefonds on detaumente des productions	No. of cases	Percentage	No.of cases	Percentage
A	20	10	100	10	100
В	Same patients	N	220		220
Total	20	10		10	

TABLE - 7-B

Showing number of cases and their percentages of pH in 48 hours.

C. marrie	Number of		Intestinal ruction		stinal oration -
Group	patients		s tube ate pH		s's tube rate pH
alphilippiness introduction about the about the second	na vinak (sakahan kan v. a. sakakan kifun sijang kana sakah saka sakah sakah sakah	No.of cases	Percentage	No.of	Percentage
C	20	13	100	7	100
D	20	12	260	8	260
Total	40	25	official members and a common consistency of the common consistency of	15	

Table 8-A & 8-B: In this study we have found that 20 patients of acute intestinal obstruction and intestinal perforation, 10 each respectively in Group-A, were showing Ryle's tube aspirate concentration range 97-99, average 98 ml/100 ml. liquid, while in Group B, the concentration range 97.5 - 99.5, average 98.5 ml/100 ml.

In 13 patients of acute intestinal obstruction and 7 patients of intestinal perforation in Group C concentration range were 97-99, (average 98 ml/100 ml.). In Group D, the concentration range were 97.5 - 98.5 (average 98.5 ml/100 ml) in 12 patients of acute intestinal obstruction and 8 patients of intestinal perforation.

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TABLE - 8-A

Showing concentration of Ryle's tube aspiration in different groups in 24 hours.

		Acute In	Acute Intestinal Obstruction	Obstru	ction	Intest	Intestinal Perforation	ora tion	
dnozg	Number of patients	No. of	Ryle's tube aspirate concentration ml/100	ube as	Ryle's tube aspirate concentration ml/100 ml.	No. of patients	Ryle's tube aspirate concentration ml/100	ube asp ation m	Ryle's tube aspirate concentration ml/100 ml
		patients	Range		Average		Range		Average
4	20	10	- 16	66	86	01	- 16	Ø) Ø)	80
	S S S S S S S S S S S S S S S S S S S	25	97.5 -	99.5	98.5	48	97.5 -	h Os	98.5
Ā	patients								man personal addressed schemes over the second schemes of the second schemes over the second scheme over the second sche
						10			
Total	20	201						etter de 10 life - 10	

TABLE - 8-B

Showing concentration of Ryle's Tube aspiration in different Groups in 48 hours.

	M. washing	Acute I	Acute Intestinal Obstruction	ruction	and the same of th	Intest	Intestinal Perforation	ion	
Group	patients	No. of	Ryle's tube aspirate concentration ml/100 ml	aspirate n ml/100 m		No. of	Ryle's tube aspirate concentration m1/100		E
			Range	Average		partents	Range	Average	
ប	20	13	66 - 26	89		7	- 76	86	
α	20	12	97.5 - 99.5	98.5		ω	97.5 - 99.5	φ (C)	
								*	
Tota1	40	52				15			1

DISCUSSION E

#### DISCUSSION

Ranitidine, Histamine receptor antagonist is being widely used mostly to reduce acid content of gastric secretion in various condition. It may also reduce gastric fluid volume to some extent.

The present study aims to across the effect of ranitidine on gastric secretion in reference to volume, pH, and concentration in post-operative patients. The study included 60 patients subjected to varied emergency surgical procedures, patients with gastro-intestinal disorders and known sensitivity to ranitidine, were not included. These patients were admitted to M.L.B. Medical College Hospital, Jhansi, in surgical wards. The diagnosis of acute intestinal obstruction as well as intestinal perforation irrespective of cause. All these patients were adequately assessed.

The patients were randomly divided into 4 groups.

- Group A received no test drug for 24 hours of
  Laparotomy acted as control.
- Group B: received ranitidine 100 mg/day in two divided doses intravenously.

- Group C: received no test drug for immediate 48 hours post-operative (acted as control).
- Group D : received ranitidine 100 mg/day in two divided doses intravenously for 2 days.

Gastro-intestinal tract, starting from oral cavity upto large intestine, secretes the intestinal juices, the volume, pH and electrolyte contents depend upon the site of secretion. The approximate volumes, secreted by the different parts of gastro-intestinal tract are as follows:

	Volume (in ml.	.) pH
Saliva	1200	6.0 - 7.0
Gastric secretion	2000	1.0 - 3.5
Pancreatic secretion	1200	8.0 - 8.3
Bile	700	7.8
Succus enterious	2000	7.8 - 8.0
Large intestine	60	7.5 - 8.0

Whenever the small intestinal obstruction occurs reflex from the small intestine causes the intestinal juices to flow backward into the stomach, and these are vomited along the stomach secretion, if they are not aspirated by the Ryle's tube. In this instance

the person loses large amount of water and electrolyte leading to dehydration.

If the obstruction is near the lower end of small intestine, then it is possible to vomit more basic than acidic substance, hence causing acidosis.

In the present study, the incidence of intestinal pathology in two sexes were found to be approximately half for male and female. Out of all the 60 patients, there were 41 male patients while the remaining 19 were female.

After statistical analysis, it was observed that the patients who were admitted to hospital for treatment of acute intestinal obstruction and intestinal perforation were distributed along a wide spectrum of age group. The children and adolescents were affected less commonly. The majority of patients who were included in this study, were in middle age group (30-49) years, constituting 43.33% of the series, on comparing the patients of acute intestinal obstruction and intestinal perforation.

It was seen that the acute intestinal obstruction was more common pathology than intestinal perforation involving 58.3% of total patients. Among the patients of acute intestinal obstruction most common age group was 40 - 49 years consisting of approximately 50% of patients.

While in intestinal perforation group again maximum number of patients were from same age group as of above i.e. 40 - 49 years.

The study performed among the patients for volume aspirated by the Ryle's tube indicates that in control group consisting of 20 patients, secreted about 1500 ml of fluid in 24 hours in cases of acute intestinal obstruction, while in cases of intestinal perforation 1750 ml of aspirate was collected in 24 hours. After giving injection ranitidine to the patients of Group-B, in the dose of 50 mg intra-venously, 12 hourly on first post-operative day only and it was found that the volume of Ryle's tube aspiration in cases of acute intestinal obstruction was 1200 ml, while in cases of intestinal perforation 1600 ml showing a clear cut decrease in volume of Ryle's tube aspirate after giving the injection of ranitidine in Group 'C'. 13 patients, which were kept as control for 48 hours study, it was seen that Ryle's tube aspiration reduced to 70% of the control volume after giving injection of Ranitidine in dose of 50 mg intravenous B.D. for two days, in cases of intestinal obstruction, while the reduction in Ryle's tube aspirate was 8.52% in cases of intestinal perforation. 

After analysing gastric aspirate for pH, it was found that the pH of both control group was in the

range of 2-3, average 2.5, while after giving ranitidine it was found markedly increased pH in all cases of study the size of pH was approximately 3 to 4 on average. It clearly indicates that after giving ranitidine, there is an increase in pH of Ryle's tube aspirate in post-operative patients, it means reduced acidic nature of the contents.

Third component of study comprises determination of solid content of Ryle's tube aspirate, show that in control group, there was about 2% of the solid content in aspirate while in the test group the amount of solid content was found to be approximately equal to the control group of cases, thereby indicating that there was hardly any change in the solid contents of the Ryle's tube aspirated fluid after giving Ranitidine injection in either of the cases.

From the above findings, it was concluded all the patients who were given the ranitidine injection either for a day or two in post-operative period, show there, clear cut decrease in volume of Ryle's tube aspirate as well as acidity while there was no change in amount of solid contents.

So, it can very well appreciated that Ranitidine is a beneficial adjuvant drug in the treatment of

post-operative cases of gastro-intestinal surgery causing reduced volume of Ryle's tube aspiration and increase pH of gastric secretion, so leading to less number of post-operative complications.

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## CONCLUSION

The present study was undertaken with the following objectives:

- To evaluate the success and effect of Ranitidine injection as an acid reducing agent in cases of acute intestinal obstruction and intestinal perforation.
- 2. To find out whether the above said method can reduce the Ryle's tube aspirate volume in all number of post-operative patients.
- 3. To evaluate the effect of Ranitidine injection on gastric aspirate solid contents.
- 4. To evaluate the result of treatment.
- 5. To discuss the finding of present study in the light of available relevant literature on the subject.
- To form a base line for the further development of the technique in the contrary.

The prospective study was conducted on 60 patients of the acute intestinal obstruction and intestinal perforation from patients attending Surgery Out Patient Department and Emergency, were admitted at M.L.B. Medical

College & Hospital, Jhansi (U.P.). Each patient was treated operatively according to the nature of disease and kept in the Surgery wards in post-operative period. Out of the 60 patients, 20 patients were selected as control, rest 20 control as well as test group and remaining 20 were used as test group.

After analysis, it was found that the male and female were equal sufferer for the disease. The age group affected more frequently was 40 - 49 years. The criteria used for evaluating the efficacy of ranitidine injection were in context of aspirated volume, pH and solid contents.

The detail of symptoms and other relevant information were noted on pre-designed and pre-tested proforma.

During the observation period, all the patients were watched for their symptoms and untoward reactions and complications. In the test group, all the patients were given injection Ranitidine in the doses of 50 mg twice a day intravenously.

In all the patients, the gastric aspirates by Ryle's tube were collected in the sterile glass bottle kept on the side of the patients.

After collecting the Ryle's tube aspirate, they were analysed for volume, pH and solid contents. It was observed that in all the patients given injection Ranitidine,

there was reduction of volume by 8 to 30% of the control group, while the increase in pH was consistant in all test patients. From 3 to 4 showing clear cut beneficial effect of the injection Ranitidine with respect to volume of Ryle's tube aspiration as well as pH, while the effect of Ranitidine on the solid contents of Ryle's tube aspiration was minimal or nil.

So we conclude that injection Ranitidine should be given in all post-operative cases of gastro-intestinal surgery due to its favourable acceptance and fine outcome leading to reduced post-operative complications.

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## SUMMARY

The present study "EFFECT OF RANITIDINE ON RYLE'S TUBE ASPIRATION IN SPECIAL REFERENCE TO VOLUME, pH AND CONCENTRATION IN LAPAROTOMY PATIENTS", conducted at M.L.B. Medical College and Hospital, Jhansi, was undertaken. It was studied in 60 patients of acute intestinal obstruction and intestinal perforation irrespective of their causes in post-operative, Ryle's tube aspiration for its volume, pH and concentration with following objectives.

- To evaluate the effect of Ranitidine injection
  as an acid reducing agent in cases of acute
  intestinal obstruction and intestinal perforation.
- 2. To find out whether the abovesaid method can reduce the Ryle's tube aspirate volume in all number of post-operative patients.
- 3. To evaluate the effect of Ranitidine injection on gastric aspirate solid contents.
- 4. To evaluate the result of treatment.
- 5. To discuss the finding of present study in the light of available relevant literature on the subject.

- 6. To form a base line for the further development of the technique in the contrary.
  - The patients were divided into 4 Groups:
- Group A Received no test drug for 24 hours of laparatomy (acted as a control).
- Group B Received injection Ranitidine 100 mg per day in two divided doses intravenously.
- Group C Received no test drug for immediate 48 hours post-operative (acted as a control).
- Group D Received injection Ranitidine 100 mg/day in two divided doses intravenously for two days.
- In the present study the incidence of intestinal pathology in two sexes were found to be approximately half for male and half for female. Out of the 60 patients, there were 41 male patients, while the remaining 19 were female patients. Age of these patients range from 10 to 59 years. The most common age group were 40 49 years. It was seen that the acute intestinal obstruction was more common pathology than the intestinal perforation, involving 58.3% of the total patients.
- While the intestinal perforation again maximum number of patients were from same age group as acute intestinal obstruction (40 to 49 years).

- In group-A 20 patients were studied, 10 cases were of acute intestinal obstruction and remaining 10 were of intestinal perforation. Post-operative Ryle's tube aspiration in cases of acute intestinal obstruction was 1500 ml in 24 hours of Laparotomy, while in cases of intestinal perforation, the average amount in 24 hours was 1750 ml.
- The average pH was 2.5 in both cases of acute intestinal obstruction and intestinal perforation.
- The concentration of solid were 2.0 gm% in both cases of acute intestinal obstruction and intestinal perforation.
- In group B, 20 same cases of group-A were studied after giving injection Ranitidine 100 mg/day in two divided doses intravenously after 24 hours of Laparotomy. The amount of Ryle's tube aspirate in acute intestinal obstruction was 1200 ml, which was less than 300 ml from group A. But in cases of intestinal perforation, the amount of Ryle's tube aspirate reduced by use of injection Ranitidine was slightly less, that was 150 ml from 1750 ml to 1600 ml.
- The change of pH by use of injection Ranitidine in cases of group-A was from 2.5 to 5.5, it means decreased acidity in both cases of acute intestinal obstruction and intestinal perforation.

- While concentration of Ryle's tube aspirate for solid contents was slightly reduced (0.5 gm%).
- In group-C, 20 patients were studied, out of which 13 cases of acute intestinal obstruction and remaining 7 were cases of intestinal perforation. This study was conducted for 48 hours of Laparotomy in which injection Ranitidine was not used. The average amount of Ryle's tube aspirate was 2500 ml in cases of acute intestinal obstruction, but in cases of intestinal perforation Ryle's tube aspirate was slightly less than acute intestinal obstruction, that was 2350 ml.
- The average pH in both cases of acute intestinal obstruction and intestinal perforation was 2.5 in 48 hours of Laparotomy, same as group-A patients.
- The solid contents of Ryle's tube aspiration in 48 hours of Laparotomy was 2.0 gm% in both cases of acute intestinal obstruction and intestinal perforation, same as group-A patients.
- Group-D, in this group 20 patients were studied, out of which 12 belongs to acute intestinal obstruction and remaining 8 were found in cases of intestinal perforation.
- Injection Ranitidine 100 mg BD intravenously was started immediately after laparotomy for two days in both cases of acute intestinal obstruction as well as

intestinal perforation. The Ryle's tube aspirate was collected for 48 hours of Laparotomy. The average amount was 1750 ml in cases of acute intestinal obstruction decreased from 2500 ml to 1750 ml. It means reduced amount was 750 ml, but in cases of intestinal perforation reduced amount was 200 ml (from 2350 to 2150 ml only).

- The change in the pH in both the cases of acute intestinal obstruction and intestinal perforation was from 2.5 to 6.5.
- So acidity was reduced more when injection Ranitidine given for 48 hours, while change in Ryle's tube aspirate concentration of solid contents in both the cases of acute intestinal obstruction and intestinal perforation from 2.0 gm% to 1.5 gm%.
- So it can be very well appreciated that

  Ranitidine is a beneficial adjuvant drug in the treatment

  of post-operative cases of gastro-intestinal surgery,

  causing reduced volume of Ryle's tube aspiration and

  increase pH of gastric secretion, thus leading to less

  number of post-operative complications.

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